REMARKS

CLAIMS REJECTIONS – 35 USC§103

Claims 7-16, 18-35 and 37-46 stand rejected under 35 U.S.C. §103 as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, Vol. 339, pages 1485-1492), Davis et al. (New England Journal of medicine, 1998, Vol. 339, pages 1493-1499), Poynard et al. (The Lancet, 1998, Vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, Vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, Vol. 42, pages 731-747). , and of claims 17 and 36 as being unpatentable over McHutchison et al., Davis et al., Poynard et al. or Reichard et al., in view of Abella et al., further in view of U.S. Patent No. 4,917,888.

Applicants are amending the application under the provisions of 34 CFR §1.116 to advance prosecution and to narrow the issues on appeal. .Applicants are amending claim 7 , and canceling claims 9, and 20 to 46 without prejudice. Upon entry of the amendment under 34 CFR §1.116, claims 7, 8, and 10 -19 remain pending.

As amended, claims 7, 8 and 10-19 are directed to methods of treating a patient having chronic HCV infection with a therapeutically effective amount of a combination therapy of interferon-alfa and ribavirin to substantially lower HCV-RNA in association with a therapeutically effective amount of Vitamin E and Vitamin C to ameliorate ribavirin-related hemolysis. Thus, applicants' claimed invention, as amended, provides an improved HCV therapy by ameloriating the ribavirin-related hemolysis throughout the duration of the combination especially in the first 4 to 12 weeks, of therapy so as to produce a sustained virological response in more patients than previously possible.

McHutchinson et al., David et al., Poynard et al., and Reichard et al. each teach the use of interferon a-2b in combination with ribavirin to treat HCV. These four references fail to teach use of antioxidants much less the specific combination of the two antioxidants, Vitamin E and Vitamin C, to treat ribavirin-induced hemolysis. Only ribavirin dose reduction is taught.

None of the deficiencies of these four references are cured by Abella et al. which discloses the evaluation of the antioxidant activity of Vitamin E in the plasma of healthy volunteers to which an oxygen free radical initiator ("AAPH") was added. Nowhere in Abella et al. is there any teaching about treating HCV patients or ribavirin -induced anemia, much less any suggestion that the combination of Vitamin E with Vitamin C would be useful in treating ribavirin –induced hemolysis in HCV patients being treated with the ribavirin-interferon alfa combination therapy. Applicants have discovered that ribavirin – induced hemolysis in HCV patients being treated with only Vitamin E and the ribavirin-interferon alfa combination therapy is **not significantly better** than ribavirin –induced hemolysis in HCV patients being treated with the ribavirin-interferon alfa combination therapy-in the absence of Vitamin E. Applicants assert that there is no motivation in the references alone or in combination to make the modification needed to bridge the gap to the claimed invention. The combined teachings of the references do not suggest the claimed invention, as amended, which specifies that a combination of two antioxidants in association with ribavirin and interferon-alfa be used to treat HCV. Only by hindsight reconstruction using applicants' claimed invention as a template can the gap from the prior art to the claimed invention be bridged.

Reconsideration and withdrawal of this ground of rejection are urged.

Claims 17 and 36 are rejected under 35 U.S.C. 103 as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, vol. 339, pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, vol. 339, pages 1493-1499,), Poynard et al. (The Lancet, 1998, vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, vol. 42, pages 731-747) as applied to claims 1-16, 17-35, and 37-46 above, and further in view of U.S. Patent 4917888 (Katre et al., 1990 and ", The '888 patent").

Applicants are amending the application by amending claims 7and 17, and by canceling claim 36.

The '888 patent discloses various pegylated proteins but cures none of the deficiencies in McHutchison, et al., Davis, et al., Poynard, et al., Reichard, et al., or Abella et al., alone or in combination.

None of these six references, alone or in combination teach use of the combination of Vitamin E with Vitamin C in association with the ribavirin-interferon alfa combination therapy to treat HCV more effectively by ameloriating the ribavirin-induced hemolysis.

Reconsideration and withdrawal of this ground of rejection are urged.

Applicants assert that the claimed invention, as amended, is in statutory compliance with 35 U.S.C.
§ 103.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

October 17, 2002
Date of Deposit

THOMAS D. HOFFMAN
Registered Representative

Signature

10/17/2002
Date of Signature

APPENDIX

Claims marked up to show the amendments

7(Twice amended). A method of treating a patient having chronic HCV infection which comprises administering to said patient a therapeutically effective amount of a combination therapy of interferon-alfa and ribavirin for a time sufficient to substantially lower HCV-RNA in association with a therapeutically effective amount of [an antioxidant] Vitamin E and Vitamin C for a time sufficient to ameliorate ribavirin-related hemolysis.